What is Claimed:

1 1.　An aldehyde having the formula:
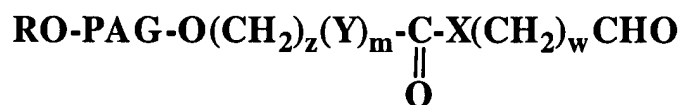
$$RO\text{-}PAG\text{-}O(CH_2)_z(Y)_m\text{-}\underset{O}{\overset{\|}{C}}\text{-}X(CH_2)_w\,CHO$$

2

3　　　　　　　　　　　　　　　　　　　　　　　　　IA

4　　　　wherein R is hydrogen or lower alkyl, X and Y are

5　　　　individually selected from $-O$ - or - NH- with the proviso

6　　　　that X is NH when m is 1 and Y is $-O\text{-}$, PAG is a divalent

7　　　　residue of polyalkylene glycol resulting from removal of the

8　　　　terminal hydroxy groups and having a molecular weight of

9　　　　from about 1,000 to about 100,000 Daltons, z is an integer

10　　　　of from 2 to 4, m is an integer of from 0 to 1, and w is an

11　　　　integer of from 2 to 8, wherein the aldehyde group is free or

12　　　　protected with a hydrolyzable aldehyde protecting group, or

13　　　　a hydrate thereof.

1 2.　The aldehyde of claim 1 wherein said residue is formed from polyethylene glycol.

1 3.　The aldehyde of claim 2 wherein the residue has a molecular weight of 5,000 to

2 50,000 Daltons.

1 4.　The aldehyde of claim 1 wherein said aldehyde has a formula:

$$RO\text{-}PAG\text{-}O(CH_2)_z\text{-}\underset{O}{\overset{\|}{C}}\text{-}NH\text{-}(CH_2)_w\,CHO$$

2

3　　　　　　　　　　　　　　　　　　　　　　　　　I-Ai
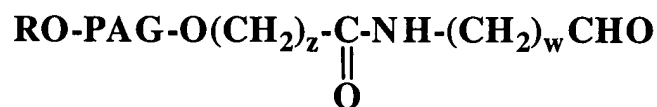
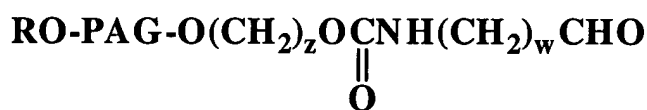4　　　　wherein R, PAG, z and w are as above.

1 5.　The aldehyde of claim 4 wherein said divalent residue is polyethylene glycol.

43

1   6.   The aldehyde of claim 5 wherein the residue has a molecular weight of 5,000 to

2   50,000 Daltons.

1   7.   The aldehyde of claim 6 wherein R is methyl and the molecular weight of the

2   residue is about 10,000 Daltons.

1   8.   The aldehyde of claim 6 wherein R is methyl, and the molecular weight of the

2   residue is 20,000 Daltons.

1   9.   The aldehyde of claim 1 wherein said aldehyde has the formula:

$$\text{RO-PAG-O(CH}_2)_z\text{O}\underset{\displaystyle \overset{\|}{\text{O}}}{\text{C}}\text{NH(CH}_2)_w\text{CHO}$$

2

3   **I-Aii.**

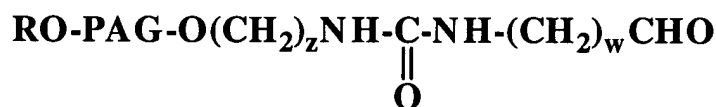4   wherein R, PAG, and w are as above, and z is an integer of

5   from 2 to 4.

1   10.   The aldehyde of claim 9 wherein said divalent residue is formed from

2   polyethylene glycol.

1   11.   The aldehyde of claim 10 wherein the residue has a molecular weight of 5,000 to

2   50,000 Daltons.

1   12.   The aldehyde of claim 11 wherein R is methyl and said residue has a molecular

2   weight of 10,000 Daltons.

1   13.   The aldehyde of claim 1 having the formula:

$$\text{RO-PAG-O(CH}_2)_z\text{NH-}\underset{\displaystyle \overset{\|}{\text{O}}}{\text{C}}\text{-NH-(CH}_2)_w\text{CHO}$$

2

3   **I-Aiii**
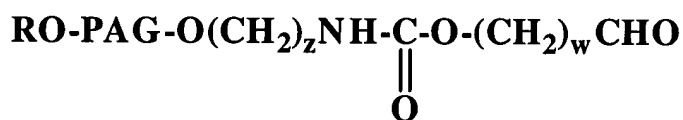
1   wherein R, PAG, and w are as above, and z is an integer of

2   from 2 to 4.

44

1   14.   The aldehyde of claim 13 wherein said divalent residue is polyethylene glycol.

1   15.   The aldehyde of claim 14 wherein the residue has a molecular weight of 5,000 to

2   50,000 Daltons.

1   16.   The aldehyde of claim 15 wherein R is methyl and the molecular weight of the

2   residue is 10,000 Daltons.

1   17.   The aldehyde of claim 1 having the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_zNH\text{-}\underset{\underset{O}{\|}}{C}\text{-}O\text{-}(CH_2)_wCHO$$

2

3   wherein R, PAG, and w are as above, and z is an integer of from 2

4   to 4.   **I-Aiv**

5   18.   The aldehyde of claim 17 wherein said divalent residue is formed from polyethylene

6   glycol.

1   19.   The compound of claim 18 wherein the residue has a molecular weight of 5,000

2   to 10,000 Daltons.

1   20.   The aldehyde of claim 19 wherein R is methyl and the molecular weight of the

2   residue is 10,000 Daltons.

1   21.   An aldehyde of the formula:

$$RO\text{-}A\text{-}OR$$

$$\left[\quad CONH(CH_2)_wCHO \quad \right]_n$$

2

3   **IB**
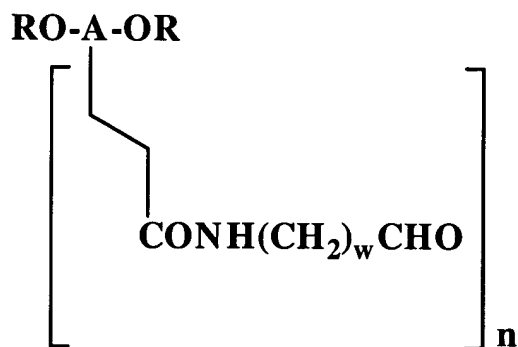
4   wherein R is hydroxyl or lower alkyl, A is a polyethylene

5   glycol residue with its two terminal hydroxy groups being

6   removed having a molecular weight of from 1,000 to

7   100,000 Daltons and having a valence of from 1 to 5, n is an

8   integer of from 1 to 5 which integer is the same as the valence

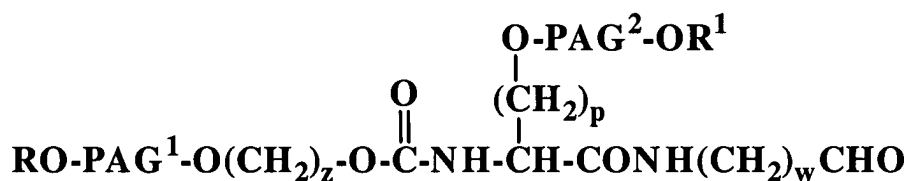9   of A, and w is an integer from 2 to 8.

1   22.   The aldehyde of claim 21 wherein A is a residue having a molecular weight of

2   from 5,000 to 50,000 Daltons.

1   23.   The aldehyde of claim 22 where n is 1.

1   24.   The aldehyde of claim 23 where the R is methyl and A has a molecular weight of

2   about 20,000 Daltons.

1   25.   The aldehyde of claim 23 wherein R is methyl and A has a molecular weight of

2   10,000 Daltons.

1   26.   An aldehyde of the formula:

$$RO\text{-}PAG^1\text{-}O(CH_2)_z\text{-}O\overset{\overset{\displaystyle O}{\|}}{\text{-}C}\text{-}NH\text{-}\overset{\overset{\displaystyle (CH_2)_p}{\big|}}{\underset{}{CH}}\text{-}CONH(CH_2)_w CHO$$

with the upper substituent $O\text{-}PAG^2\text{-}OR^1$

2

3   IC

4   wherein PAG[1] and PAG[2] are independently divalent residues

5   of poly lower alkylene glycol resulting from removal of the

6   two terminal hydroxy groups with the PAG[1] and PAG[2]

7   residues having a combined molecular weight of from 1,000

8   to 100,000 Daltons, R and R[1] are individually lower alkyl or

9   hydrogen, z is an integer of from 2 to 4, m is an integer of

10   from 0 to 1, and w is an integer of from 2 to 8, wherein the

11   aldehyde group is free or protected with a hydrolyzable

12   aldehyde protecting group, or a hydrate thereof.

1   27.   The aldehyde of claim 26 wherein said R is methyl, PAG^1 and PAG^2 are formed

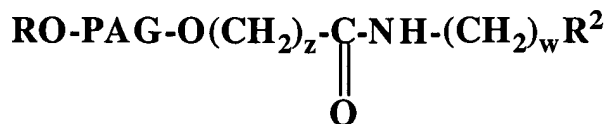2   from polyethylene glycol residues.

1   28.   The aldehyde of claim 27 wherein R is methyl and PAG^1 and PAG^2 both have a

2   molecular weight of 5,000 to 50,000 Daltons.

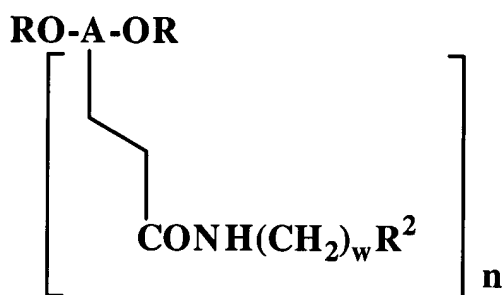1   29.   A compound of the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_z(Y)_m\text{-}\underset{\displaystyle \overset{\|}{O}}{C}\text{-}X(CH_2)_w R^2$$
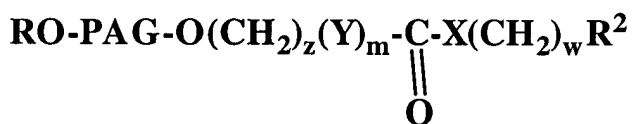
2

3   wherein R is hydrogen or lower alkyl, R^2 is -

4     $CH(OH)CH(OH)R_{13}$ wherein R_{13} is hydrogen, alkyl, or

5   phenyl, X and Y are individually selected from -O- or -NH-

6   with the proviso that X is NH when m is 1 and Y is -O-, PAG

7   is a divalent residue of polyalkylene glycol resulting from

8   removal of the terminal hydroxy groups and having a

9   molecular weight of from about 1,000 to about 100,000

10   Daltons, z is an integer of from 2 to 4, m is an integer of from

11   0 to 1, and w is an integer of from 2 to 8.

1   30.   The conjugate of claim 29 where said conjugate has the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_z\text{-}\underset{\displaystyle \overset{\|}{O}}{C}\text{-}NH\text{-}(CH_2)_w R^2$$

2

3   wherein PAG, R, R^2, z and w are as above.

1   31.   A compound of the formula:

2

$$RO\text{-}A\text{-}OR$$

$$\left[\begin{array}{c} \\ CONH(CH_2)_w R^2 \end{array} \right]_n$$

3

4   wherein R is hydrogen or lower alkyl, R^2 is -

5       $CH(OH)CH(OH)R_{13}$ wherein R_{13} is hydrogen, alkyl, or

6   phenyl, A is a polyethylene glycol residue with its two

7   terminal hydroxy groups being removed having a molecular
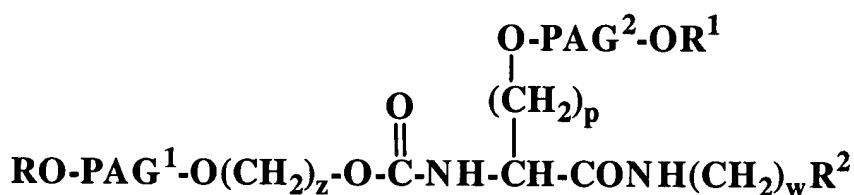
8   weight of from 1,000 to 100,000 Daltons and having a

9   valence of from 1 to 5, n is an integer of from 1 to 5 which

10   integer is the same as the valence of A, and w is as integer of

11   from 2 to 8.

1   32.   A compound of the formula:

$$O\text{-}PAG^2\text{-}OR^1$$
$$\overset{\displaystyle O}{\overset{\displaystyle \|}{}} \quad \overset{\displaystyle (CH_2)_p}{|}$$
$$RO\text{-}PAG^1\text{-}O(CH_2)_z\text{-}O\text{-}C\text{-}NH\text{-}CH\text{-}CONH(CH_2)_w R^2$$

2

3   wherein PAG^1 and PAG^2 are independently divalent residues

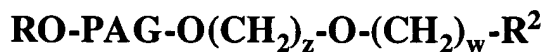4   of poly lower alkylene glycol resulting from removal of the

5   two terminal hydroxy groups with the PAG^1 and PAG^2

6   residues having a combined molecular weight of from 1,000

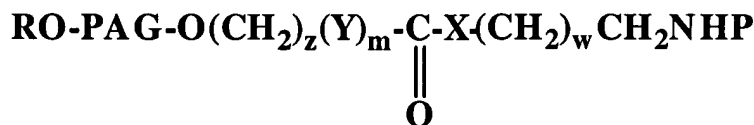7   to 100,000 Daltons, R and R^1 are individually lower alkyl or

48

8 hydrogen, R^2 is $CH(OH)CH(OH)R_{13}$ wherein R_{13} is

9 hydrogen, alkyl, or phenyl, w is an integer from 2 to 8, p is an

10 integer of from 1 to 5, and z is an integer of from 2 to 4.

1 33. A compound of the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_z\text{-}O\text{-}(CH_2)_w\text{-}R^2$$

3 wherein R is lower alkyl or hydrogen, R^2 is -

4 $CH(OH)CH(OH)R_{13}$ wherein R_{13} is hydrogen, alkyl, or

5 phenyl, PAG is the divalent residue of polyethylene glycol

6 resulting from removal of the two terminal hydroxy groups

7 having a molecular weight of from 1,000 to 100,000 Daltons,

8 z is a integer of from 2 to 4 and w is an integer of from 2 to 8.

1 34. A conjugate of the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_z(Y)_m\text{-}\underset{\displaystyle O}{\overset{\displaystyle \|}{C}}\text{-}X\text{-}(CH_2)_w\,CH_2NHP$$

3 **III-A**

4 wherein P is the residue of a protein with its amino group

5 removed, R is hydrogen or lower alkyl, X and Y are

6 individually selected from -O- or -NH with the proviso that

7 X is NH when Y is −O-, PAG is a divalent residue of

8 polyalkylene glycol resulting from removal of the terminal

9 hydroxy groups, having a molecular weight of from 1,000 to

10 100,000 Daltons, z is an integer of from 2 to 4, m is an

11 integer of from 0 to 1, and w is an integer of from 2 to 8.

1   35.   The conjugate of claim 34 where said conjugate has the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_z\text{-}\underset{\underset{O}{\|}}{C}\text{-}NH\text{-}(CH_2)_w CH_2NHP$$

2

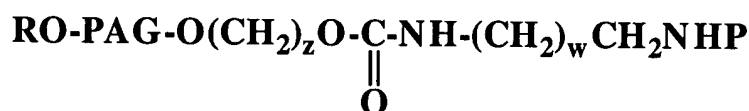3   III-E
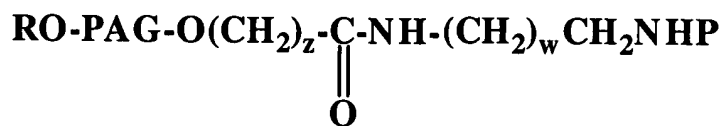
4   wherein P, R, PAG, z and w are as above.

1   36.   The conjugate of claim 35 wherein PAG is formed from polyethylene glycol

2 having a molecular weight of from 5,000 to 50,000.

1   37.   The conjugate of claim 36 where said P is G-CSF, EPO, IFN-α, IFN-β or

2 Hemoglobin.

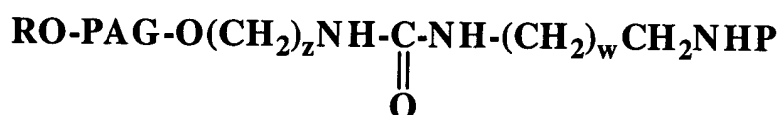1   38.   The conjugate of claim 34 wherein said conjugate has the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_zO\text{-}\underset{\underset{O}{\|}}{C}\text{-}NH\text{-}(CH_2)_w CH_2NHP$$

2

3   III-F

4   wherein P, R, PAG, and w are as above, and z is an integer of from

5   2 to 4

1   39.   The conjugate of claim 38 wherein PAG is polyethylene glycol having a

2 molecular weight of from 5,000 to 50,000.

1   40.   The conjugate of claim 39 where said P is G-CSF, EPO, IFN-α, IFN-β or

2 Hemoglobin.

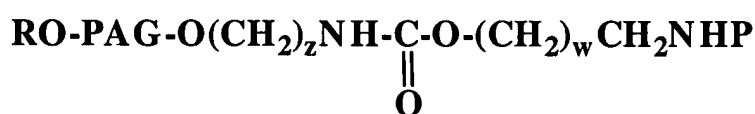1   41.   The conjugate of claim 34 wherein said conjugate has the formula:

2

$$RO\text{-}PAG\text{-}O(CH_2)_zNH\text{-}\underset{\underset{O}{\|}}{C}\text{-}NH\text{-}(CH_2)_w CH_2NHP$$

3

4   III-G

5   wherein P, R, PAG, and w are as above, and z is an integer of from

6   2 to 4.

1   42.   The conjugate of claim 41 wherein PAG is polyethylene glycol having a molecular

2   weight of from 5,000 to 50,000.

1   43.   The conjugate of claim 42 where said P is G-CSF, EPO, IFN-α, IFN-β or

2   Hemoglobin.

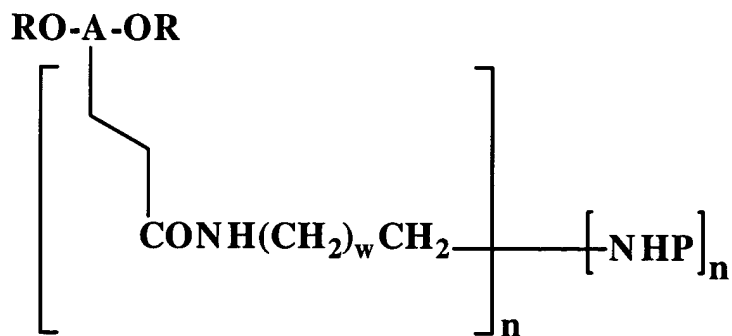1   44.   The conjugate of claim 34 wherein said conjugate has the formula:

$$RO\text{-}PAG\text{-}O(CH_2)_z NH\text{-}\underset{\underset{O}{\|}}{C}\text{-}O\text{-}(CH_2)_w CH_2 NHP$$

2

3   III-H

1   wherein P, R, PAG, and w are as above, and z is an integer of from

2   2 to 4.

1   45.   The conjugate of claim 44 wherein PAG is polyethylene glycol having a molecular

2   weight of from 5,000 to 50,000 Daltons.

1   46.   The conjugate of claim 45 where said P is G-CSF, EPO, IFN-α, IFN-β or

2   Hemoglobin.

1   47.   A conjugate of the formula:

RO-A-OR

$$\left[\begin{array}{c} \\ CONH(CH_2)_w CH_2\end{array}\right]_n \!\!-\!\!\left[NHP\right]_n$$

2   III-B

3   wherein P is a residue of a protein with its amino group
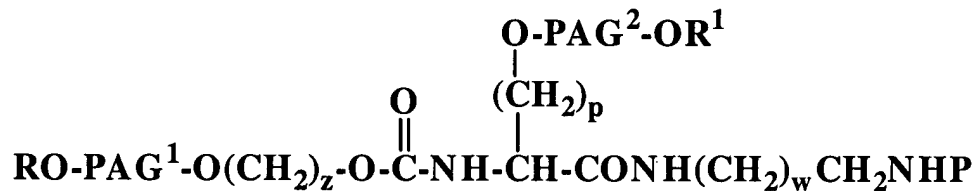
4   removed,

5   R is hydrogen or lower alkyl, A is a polyethylene glycol

6   residue with its two terminal hydroxy groups being removed

7   having a molecular weight of from 1,000 to 100,000 Daltons

8   and having a valence of from 1 to 5, n is an integer of from 1

9   to 5 which integer is the same as the valence of A, and which

10   integer is the same as the number of proteins P, w is as

11   above.

1   48.   The conjugate of claim 47 where n is 1.

1   49.   The conjugate of claim 47 where A is polyethylene glycol residue.

1   50.   The conjugate of claim 49 wherein PAG is polyethylene glycol having a molecular

2   weight of from 5 to 50,000 Daltons.

1   51.   A conjugate with the formula:

$$\begin{array}{c} \text{O-PAG}^2\text{-OR}^1 \\ | \\ \text{O} \qquad (\text{CH}_2)_p \\ \| \qquad\quad | \\ \text{RO-PAG}^1\text{-O(CH}_2)_z\text{-O-C-NH-CH-CONH(CH}_2)_w\,\text{CH}_2\text{NHP} \end{array}$$

3   III-C

4   wherein P is a residue of a protein with its amino group

5   being removed, PAG^1 and PAG^2 are independently divalent

6   residues of poly lower alkylene glycol resulting from removal

7   of the two terminal hydroxy groups and with the PAG^1 and

8   PAG^2 residues having a combined molecular weight of from

9   1,000 to 100,000 Daltons, R and R^1 are individually lower

10   alkyl or hydrogen, w is an integer of from 2 to 8, p is an

11   integer of from 1 to 5, and z is an integer of from 2 to 4.

52

1   52.   The conjugate of claim 51 where PAG^1 and PAG^2 are each polyethylene glycol

2   having a combined molecular weight from 5,000 to 50,000.

1   53.   A conjugate of the formula

$$RO\text{-}PAG\text{-}O(CH_2)_zO\text{-}(CH_2)_wCH_2NHP$$

2   III-D
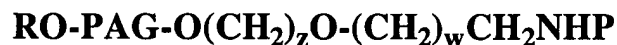
3   wherein P is a residue of a protein with an amino group

4   being removed, PAG is a divalent residue of a poly lower

5   alkylene glycol resulting from removal of the two terminal

6   hydroxy groups having a molecular weight of from 1,000 to

7   100,000 Daltons, R is lower alkyl or hydrogen, w is an

8   integer from 2 to 8 and z is an integer from 2 to 4.

1   54.   The conjugate of claim 53 where PAG is a polyethylene glycol residue.

1   55.   The conjugate of claim 54 where PAG has a molecular weight of from 5,000 to

2   50,000 Daltons.

1   56.   A process for producing an aldehyde of the formula
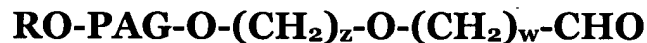
2                      $$RO\text{-}PAG\text{-}O\text{-}(CH_2)_z\text{-}O\text{-}(CH_2)_w\text{-}CHO$$

3   wherein R is lower alkyl, PAG is a divalent residue of

4   polyalkylene glycol resulting from removal of the terminal

5   hydroxy groups, having a molecular weight of from 1,000 to

6   100,000 Daltons, z is an integer of from 2 to 4, and w is an

7   integer of from 2 to 8;

8   from a hydroxy compound of the formula

9                    $$RO\text{-}PAG\text{-}O\text{-}(CH_2)_z\text{-}OH$$

53
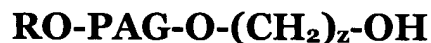
10   wherein R, PAG are as above, and z is an integer of from 2 to

11   4; comprising esterifying said hydroxy compound to form an

12   ester of the formula

13   **RO-PAG-O-$(CH_2)_z$-OL**

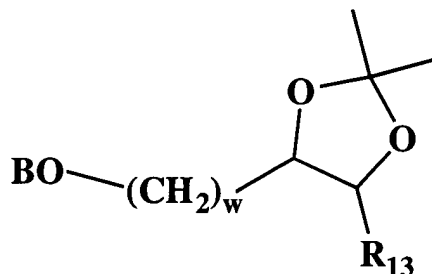14   wherein R and PAG are as above and OL is a sulfonic acid

15   ester;

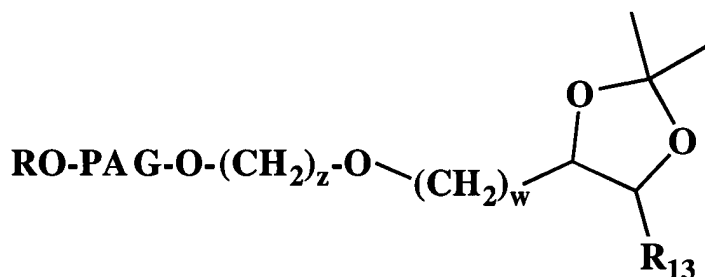16   by reacting said hydroxy compound with a sulfonating agent having the formula

17   **HaloL**

18   wherein L is a sulfonyl leaving group and Halo is a halogen;

19   to form said sulfonate ester, and reacting said ester with an acetonide of the formula

20

21   wherein R_{13} is hydrogen, alkyl, or phenyl, w is as above and B

22   is an alkali metal;

23   to form a polymeric acetonide of the formula

24

25

26

27

28

29

30

$$RO\text{-}PAG\text{-}O\text{-}(CH_2)_z\text{-}O\text{-}(CH_2)_w \begin{array}{c} \\ \end{array}$$

31

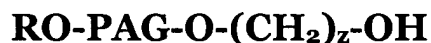32   wherein R, PAG, R_{13}, z and w are as above;

33 and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove

34 the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation

35 with a periodate oxidizing agent to form said aldehyde.

1   57. A process for producing an aldehyde of the formula
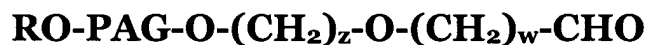
2   **RO-PAG-O-(CH$_2$)$_z$-O-(CH$_2$)$_w$-CHO**

3   wherein R is lower alkyl, PAG is a divalent residue of

4   polyalkylene glycol resulting from removal of the terminal

5   hydroxy groups, having a molecular weight of from 1,000 to

6   100,000 Daltons, z is an integer of from 2 to 4, and w is an
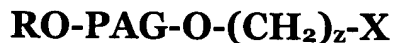
7   integer of from 2 to 8;

8 from a hydroxy compound of the formula

9   **RO-PAG-O-(CH$_2$)$_z$-OH**

10   wherein R, PAG and z are as above;

11 comprising halogenating said hydroxy compound to form a halide of the formula

55

12   **RO-PAG-O-(CH₂)ᵤ-X**

13   by reacting said hydroxy compound with a halogenating agent having the formula

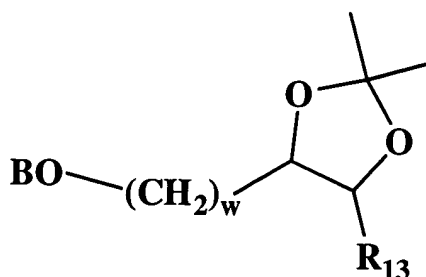14   **X₂SO**

15   wherein X is a halogen;

16   to form said halide, and reacting said halide with an acetonide of the formula

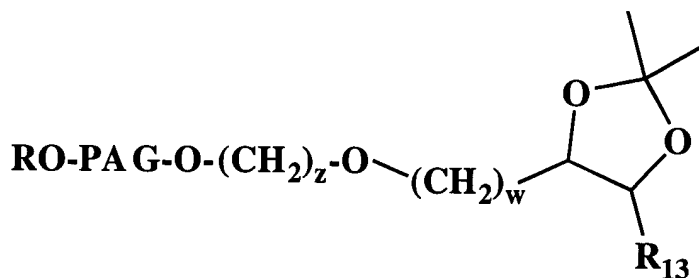

17

18   wherein R_{13} is hydrogen, alkyl, or phenyl, w is as above and B

19   is an alkali metal;

20   to form a polymeric acetonide of the formula

21   wherein R, R_{13}, PAG, z and w are as above;
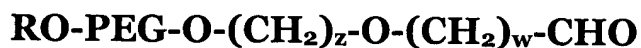
22   and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove

23   the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation

24   with a periodate oxidizing agent to form said aldehyde.

1   58.   A process for producing an aldehyde of the formula

2   **RO-PEG-O-(CH₂)ᵤ-O-(CH₂)ᵥ-CHO**

3   wherein PEG is a divalent residue of polyethylene glycol

4   resulting from removal of the terminal hydroxy groups,

5   having a molecular weight of from 1,000 to 100,000 Daltons,

6   and w is an integer of from 2 to 8, and z is an integer of from

7   2 to 4.

$$BO-(CH_2)_w \overset{\displaystyle O}{\underset{\displaystyle R_{13}}{\diagdown}}$$

8
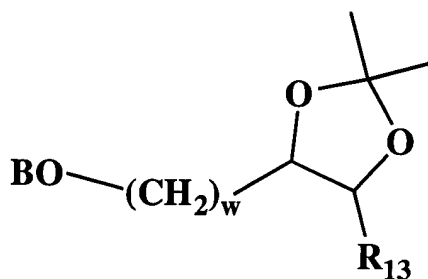
9   from an acetonide of the formula

10

11   wherein B is an alkali metal, and R_{13} and w are as above;

$$HO\text{-}PEG\text{-}O\text{-}(CH_2)_z\text{-}O\diagdown(CH_2)_w \overset{\displaystyle O}{\underset{\displaystyle R_{13}}{\diagdown}}$$
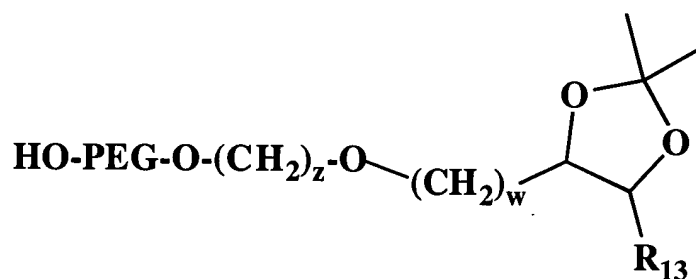
12   comprising reacting said acetonide with ethylene oxide by passing liquid ethylene oxide

13   into an organic solution containing the acetonide under polymerization conditions to

14   form the hydroxy acetonide compound of the formula

15   wherein PEG, R_{13}, z and w are as above;

57

$$\text{RO-PEG-O-(CH}_2)_z\text{-O-(CH}_2)_w\text{-}\underset{R_{13}}{\text{[dioxolane acetonide ring]}}$$
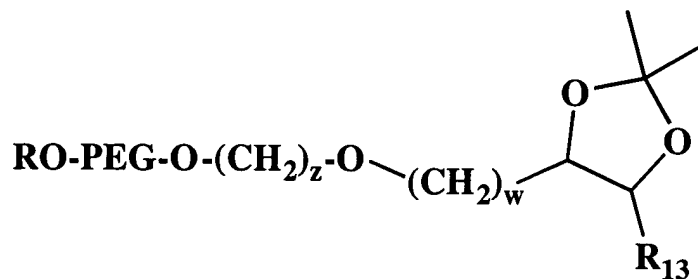
16   etherifying said hydroxy acetonide with a lower alkyl halide to form a polymeric

17   acetonide of the formula

18

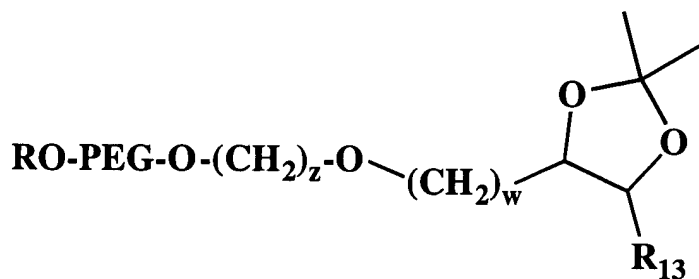19   wherein R is lower alkyl, and PEG, R_{13}, z and w are as above;

20   and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove

21   the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation

22   with a periodate oxidizing agent to form said aldehyde.

1   59.   A process for producing an aldehyde of the formula

2   **RO-PEG-O-(CH₂)z-O-(CH₂)w-CHO**

3   wherein PEG is a divalent residue of polyethylene glycol

4   resulting from removal of the terminal hydroxy groups,

5   having a molecular weight of from 1,000 to 100,000 Daltons,

6   z is an integer of from 2 to 4, and w is an integer of from 2 to

7   8;

8   from a polymeric acetonide of the formula

$$\text{RO-PEG-O-}(CH_2)_z\text{-O}\diagdown_{(CH_2)_w}\underset{R_{13}}{\overset{O\diagup\diagdown\ \diagup O}{\diagup}}$$

9

10   wherein R, PEG, R_{13}, z and w are as above;

11   and thereafter hydrolyzing said polymeric acetonide under acid conditions to remove

12   the acetonide group, and thereafter subjecting said hydrolyzed acetonide to oxidation

13   with a periodate oxidizing agent to form said aldehyde.

1   60.   An aldehyde of the formula:

2   **RO-PAG-O-$(CH_2)_z$-O-$(CH_2)_w$-CHO**
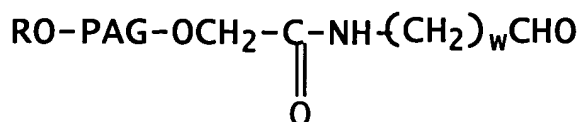
3   wherein R is lower alkyl, PAG is a divalent residue of

4   polyalkylene glycol resulting from removal of the terminal

5   hydroxy groups, having a molecular weight of from 1,000 to

6   100,000 Daltons, z is an integer of from 2 to 4, and w is an

7   integer of from 2 to 8.

8   61.   The aldehyde of claim 60 wherein said divalent residue is formed from

9   polyethylene glycol.

1   62.   The aldehyde of claim 61 wherein the residue has a molecular weight of 5,000 to

2   50,000 Daltons.

1   63.   The aldehyde of claim 62 wherein R is methyl and said residue has a molecular

2   weight of 20,000 Daltons.

1   64.   The aldehyde of formula:

$$\text{RO-PAG-OCH}_2\text{-}\underset{\underset{O}{\|}}{C}\text{-NH-}(\text{CH}_2)_w\text{CHO}$$

2

3   **I-Ai**

4   wherein R is hydrogen or lower alkyl, PAG is a divalent

5   residue of polyalkylene glycol resulting from removal of the

6   terminal hydroxy groups and having a molecular weight of

7   from about 1,000 to 100,000 Daltons and w is an integer of

8   from 2 to 8.

1   65.   The aldehyde of claim 64 wherein said divalent residue is polyethylene glycol.

1   66.   The aldehyde of claim 65 wherein the residue has a molecular weight of 5,000 to

2   50,000 Daltons.

1   67.   The aldehyde of claim 66 wherein R is methyl and the molecular weight of the

2   residue is about 10,000 Daltons.

1   68.   The aldehyde of claim 67 wherein R is methyl, and the molecular weight of the

2   residue is 20,000 Daltons.

1   69.   The conjugate of the formula:

$$\text{RO-PAG-OCH}_2\text{-}\underset{\underset{O}{\|}}{C}\text{-NH-}(\text{CH}_2)_w\text{R}_2$$

2
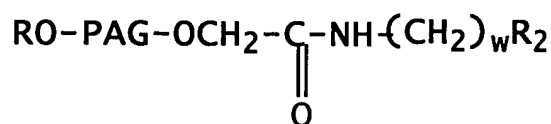
3   wherein PAG is a divalent residue of polyalkylene glycol

4   resulting from removal of the terminal hydroxy groups and

5   having a molecular weight of from about 1,000 to about

6   100,000 Daltons, R is hydrogen or lower alkyl, R^2 is -

60

7   CH(OH)CH(OH)R_{13} wherein R_{13} is hydrogen, alkyl, or

8   phenyl, and w is an integer of from 2 to 8 and are as above.

1   70.   The conjugate of the formula:

$$RO-PAG-OCH_2-\underset{\underset{O}{\|}}{C}-NH\text{-}(CH_2)_wCH_2NHP$$

2

3   **III-E**
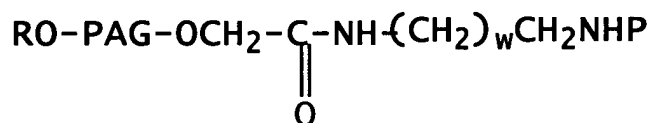
4   wherein P is the residue of a protein with its amino group removed, R is

5   hydrogen or lower alkyl, PAG is a divalent residue of polyalkylene glycol

6   resulting from removal of the terminal hydroxy groups, having a molecular

7   weight of from 1,000 to 100,000 Daltons, and w is an integer of from 2 to

8   8 and are as above.

1   71.   The conjugate of claim 70 wherein PAG is formed from polyethylene glycol

2 having a molecular weight of from 5,000 to 50,000.

1   72.   The conjugate of claim 71 where said P is G-CSF, EPO, IFN-α, IFN-β or

2 Hemoglobin.